

UNITED STATES PATENT AND TRADEMARK OFFICE
CERTIFICATE OF CORRECTION

PATENT NO. : 6,783,965 B1
APPLICATION NO. : 09/501730
DATED : August 31, 2004
INVENTOR(S) : Sherman et al.

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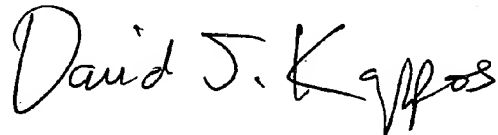
It is certified that error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

On the Title page of the patent, please replace exemplary drawing FIG. 1 with corrected FIG. 1.

Also, please replace FIG. 1 and FIG. 5 with corrected replacement figures attached herein.

Signed and Sealed this

First Day of September, 2009

A handwritten signature in black ink, reading "David J. Kappos". The signature is written in a cursive, flowing style with a large initial 'D' and a stylized 'K'.

David J. Kappos
Director of the United States Patent and Trademark Office

(12) **United States Patent**
Sherman et al.

(10) **Patent No.:** **US 6,783,965 B1**
(45) **Date of Patent:** ***Aug. 31, 2004**

(54) **AGGREGATE-FREE URATE OXIDASE FOR PREPARATION OF NON-IMMUNOGENIC POLYMER CONJUGATES**

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(73) **Assignee:** Mountain View Pharmaceuticals, Inc., Menlo Park, CA (US)

(*) **Notice:** Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 0 days.

This patent is subject to a terminal disclaimer.

(21) **Appl. No.:** 09/301,730

(22) **Filed:** Feb. 10, 2000

(51) **Int. Cl.:** C12N 9/04; C12N 15/00; A61K 38/44; C07K 1/00; C07H 21/04

(52) **U.S. Cl.:** 435/190; 435/191; 435/440; 424/94.4; 536/23.2; 530/350

(58) **Field of Search:** 435/190, 191, 435/440, 170; 424/94.4, 94.6; 536/23.2; 530/350, 413

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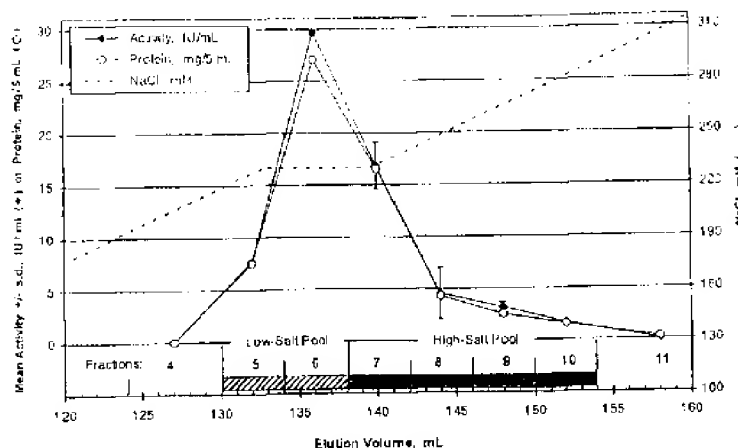
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(57) **ABSTRACT**

A naturally occurring or recombinant protein, especially a mutein of porcine urate oxidase (uricase), that is essentially free of large aggregates can be rendered substantially non-immunogenic by conjugation with a sufficiently small number of strands of polymer such that the bioactivity of the protein is essentially retained in the conjugate. Such conjugates are unusually well suited for treatment of chronic conditions because they are less likely to induce the formation of antibodies and/or accelerated clearance than are similar conjugates prepared from protein preparations containing traces of large aggregates.

30 Claims, 6 Drawing Sheets

UV Assay of Uricolytic Activity in Fractions from Mono Q Chromatography of PKS Uricase
(Protein Based on Size Exclusion HPLC)



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UV Assay of Uricolytic Activity in Fractions from Mono Q Chromatography of PKS Uricase
(Protein Based on Size-Exclusion HPLC)

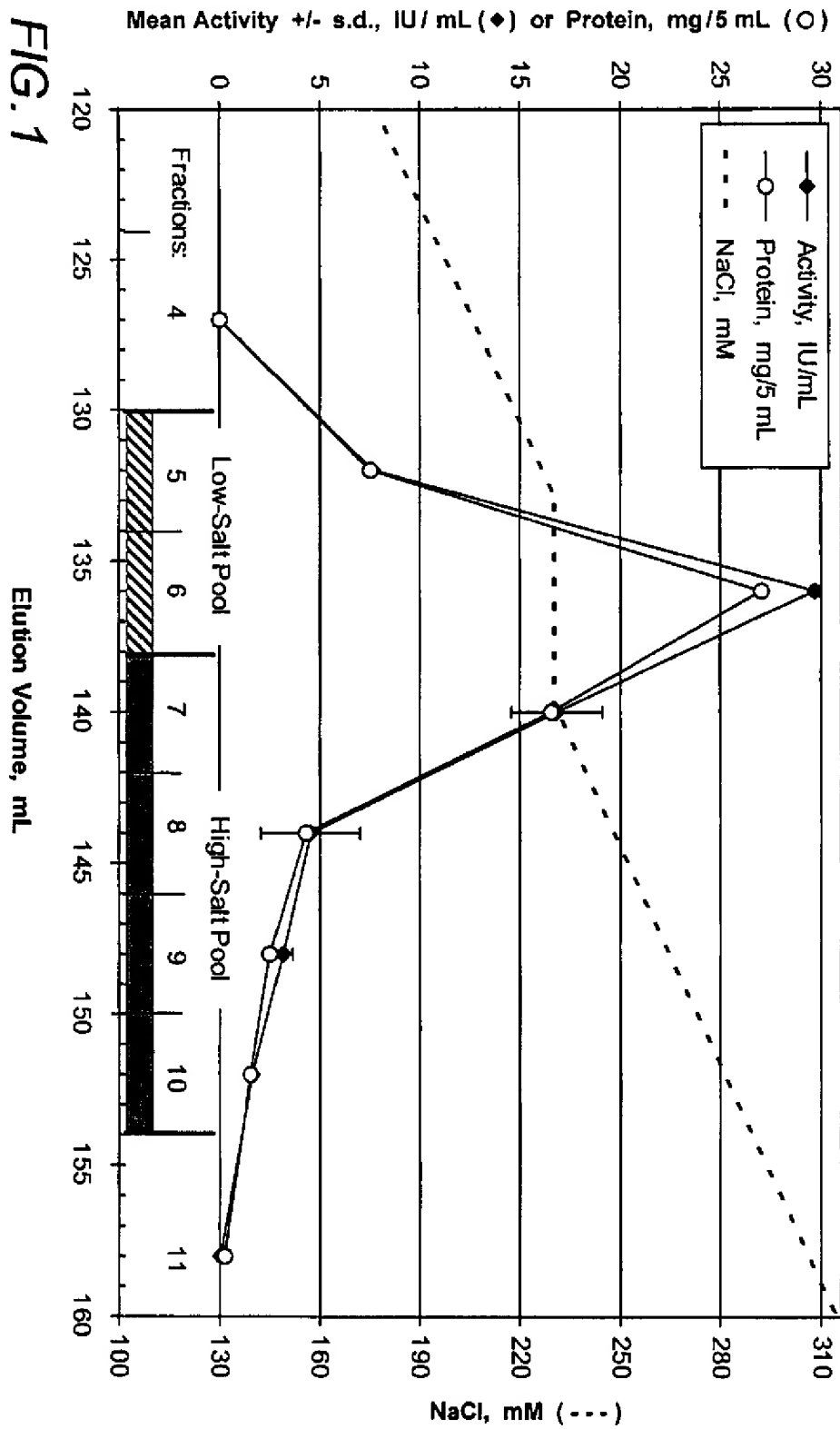
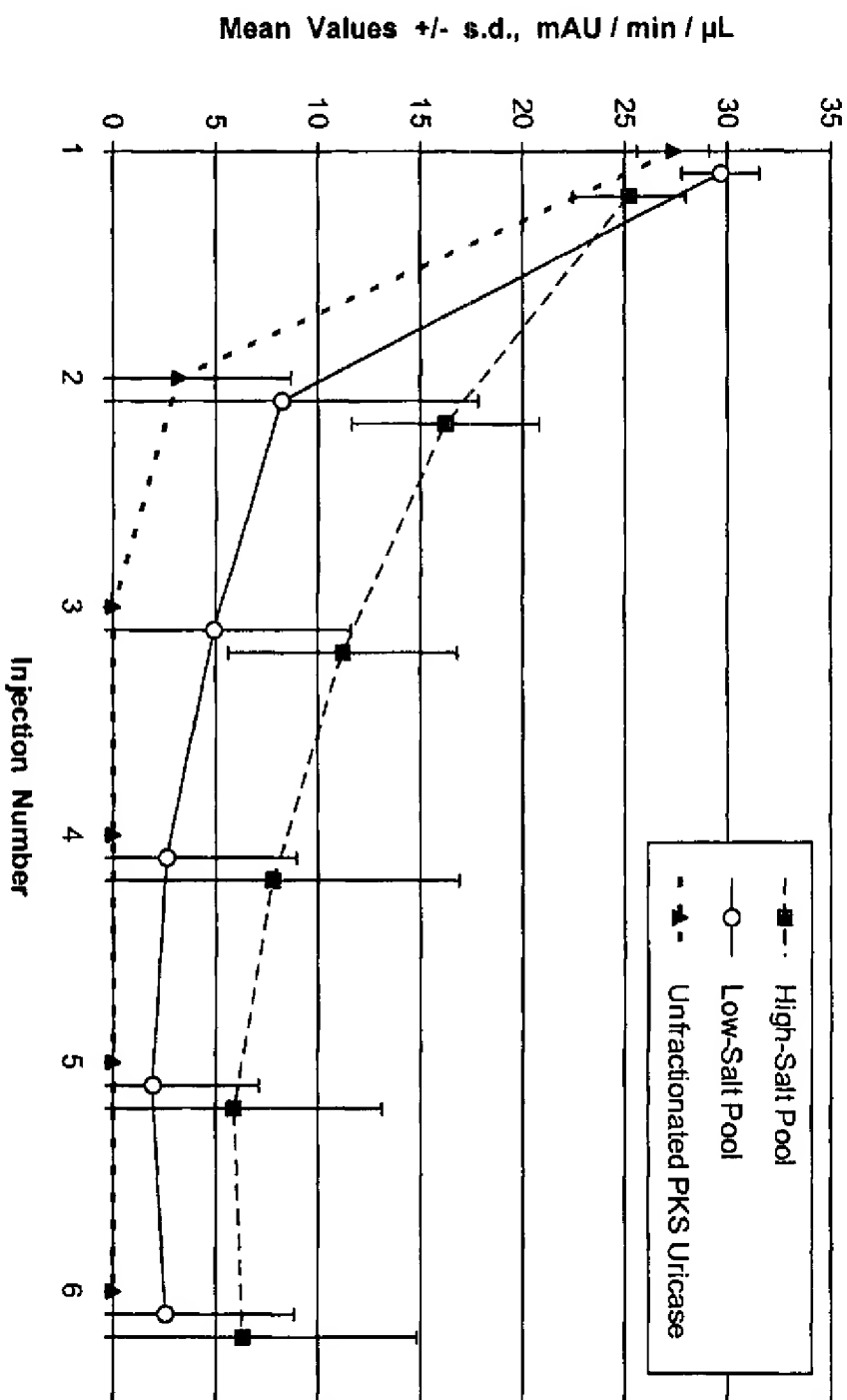


FIG. 5

**UV Uricase Assays of Sera from Mice Injected with 6 x 10-kDa PEG
Conjugates of PKS Uricase or of Pools from Mono Q Column Fractions
(Mice Were Bled 24 Hours after Each Weekly Injection.)**



Data for the Low-Salt and High-Salt Pools were shifted on the x-axis by 0.1 and 0.2 units, respectively.